

cholaminergic neurones seems unlikely since amphetamine (0.5–2.0 mg/kg, i.v.) does not inhibit raphé units under these conditions.

I am grateful for the help and encouragement of Professor D. W. Straughan. This work was supported by a Medical Research Council grant to Professor D. W. Straughan.

REFERENCES

- AGHAJANIAN, G. K., FOOTE, W. E. & SHEARD, M. H. (1968). Lysergic acid diethylamide: sensitive neuronal units in the midbrain raphé. *Science, N. Y.*, **161**, 706.
 AGHAJANIAN, G. K., FOOTE, W. E. & SHEARD, M. H. (1970). Action of psychotogenic drugs on single midbrain raphé neurons. *J. Pharmac. exp. Ther.*, **171**, 178.
 FOOTE, W. E., SHEARD, M. H. & AGHAJANIAN, G. K. (1969). Comparison of effects of LSD and amphetamine on midbrain raphé units. *Nature, Lond.*, **222**, 567.
 ROSS, S. B. & RENYI, A. L. (1969). Inhibition of the uptake of tritiated 5-hydroxytryptamine in brain tissue. *Eur. J. Pharmac.*, **7**, 270.

Effects of chronic and acute cannabis treatment upon thiopentone anaesthesia in rabbits

W. D. M. PATON and DIANA M. TEMPLE*

Department of Pharmacology, University of Oxford, Oxford OX1 3QT

Four groups of rabbits were used. Each of the first group, 'acute cannabis', received 50 mg/kg crude cannabis (100 mg/ml in saline, stabilized with 40 mg/ml of Tween 80) intravenously 45 min before anaesthesia. Each of the 'chronic cannabis' group received 50 mg/kg crude cannabis subcutaneously daily for 63 days until 5 days before thiopentone administration. The 'chronic Tween' group received the same daily doses of Tween 80 as the chronic cannabis group. The control animals were untreated. The cannabis used was obtained by removal of ethanol from Tincture of Cannabis (Gill, Paton & Pertwee, 1970).

Sodium thiopentone (5%) was injected intravenously into the rabbit ear vein over approximately 2 min, until both corneal reflex and reaction to a standard ear-pinch had just ceased. Recovery was followed by recording, for each animal, the time from the midpoint of the injection to the appearance of each of the following signs: (1) slight reaction to ear-pinch and corneal touch; (2) pronounced reactions

TABLE 1.

Group	No. of rabbits	Dose of thiopentone (mg/kg)	Duration of injection (min)	Time (mean value in min \pm S.E.) to reach recovery stage (see text):					
				1	2	3	4	5	6
Control	3	30	1.9 ± 0.2	3.8 ± 0.4	6.1 1.0	—	8.8 2.7	11.1 0.9	20.6 2.7
Acute cannabis	3	22.3 ± 2.6	2.1 ± 0.2	7.3 ± 0.9	11.2 1.9	—	6.2 0.6	16.7 1.8	24.8 3.5
	1	30.0*	2.5	20.0	35.0	—	44.0	58.0	66.0
Chronic cannabis	3	23.7 ± 0.3	1.8 ± 0.1	5.1 ± 0.5	6.7 0.3	9.4 2.1	7.0 1.0	12.3 4.0	19.2 3.1
	6†	23.9 ± 0.9	1.8 ± 0.2	4.6 ± 0.5	5.9 0.4	7.6 1.7	7.9 1.0	10.2 2.0	15.8 2.3
Chronic Tween	3	31.7 ± 1.2	2.3 ± 0.2	5.1 ± 0.6	7.5 0.5	9.8 0.7	—	12.3 0.8	15.7 1.6
	4†	31.8 ± 0.8	2.2 ± 0.2	4.9 ± 0.5	6.9 0.7	8.0 1.8	5.5	11.7 1.4	16.8 1.6

* This dose passed the normal end-point. † Individual rabbits received a second treatment with thiopentone 3 or more days after the first.

to these; (3) spontaneous blink; (4) eye movement; (5) momentary lifting of the head; (6) sitting up. The mean recovery rates for all groups were compared using *t* tests.

The results are summarized in Table 1. The acute cannabis and chronic cannabis groups required a mean dose of thiopentone to reach the anaesthetic endpoint which was 26-27% smaller than for their respective untreated or chronic Tween controls. The latter did not differ significantly in the dose required. The rate of recovery was indistinguishable in all four groups of animals. One acute cannabis treated animal, however, which was given the same dose of thiopentone as the control group, being therefore more deeply anaesthetized, took 3 times longer to recover.

It is concluded that cannabis potentiates thiopentone anaesthesia in the rabbit, and that the potentiation lasts at least 5 days longer than a period of chronic cannabis administration.

REFERENCE

GILL, E. W., PATON, W. D. M. & PERTWEE, R. G. (1970). Preliminary experiments on the chemistry and pharmacology of cannabis. *Nature, Lond.*, **228**, 134-136.

Brain monoamines and the increase in motor activity in the rat after amphetamine

H. C. GULDBERG and C. A. MARSDEN*

Department of Pharmacology, University of Bergen, Bergen, Norway

Unilateral lesions in the nigrostriatal dopamine pathway of the rat induce asymmetric posture (Andén, Dahlström, Fuxe & Larsson, 1966) which can be converted into vigorous rotation towards the lesioned side by the administration of amphetamine (Ungerstedt, 1969). The present study attempts to demonstrate whether 5-hydroxytryptamine and/or noradrenaline have a function in amphetamine-induced rotational motor activity.

Electrolytic lesions were placed in the following brain areas of albino rats: left substantia nigra, medial raphé nucleus and the left or right mesencephalic reticular formation in the area of the cerebellar-rubral tract. In one group of rats a lesion was placed in the substantia nigra and another in the medial raphé nucleus of the same animal. The rats were observed for signs of asymmetry for up to 42 days after the operations and were administered amphetamine (3 mg/kg i.p.) on three occasions during this period. At the end of the observation period the animals were killed and the concentrations of dopamine, 5-hydroxytryptamine and noradrenaline were determined biochemically in the striatum, hippocampus and forebrain cerebral cortex. Brain sections (25 μ m) were stained for the localization of acetylcholinesterase to verify the sites of the lesions.

Rats with lesions in the substantia nigra had reduced dopamine concentrations in the striatum on the lesioned side. Lesions in the medial raphé nucleus reduced the 5-hydroxytryptamine content of the striatum (by 70%), hippocampus (by 62%) and the cerebral cortex (by 55%), while the dopamine in the striatum was unaffected. Rats with lesions in both the left substantia nigra and the medial raphé nucleus often showed marked asymmetry either ipsi- or contralateral to the lesion in the substantia nigra. This asymmetry was potentiated by amphetamine. Rats with a lesion in the medial raphé nucleus were hyperactive but showed no consistent asymmetry, although several showed spontaneous asymmetrical rotation either moving